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CLINICAL PROCEEDINGS

of the

CHILDREN'S HOSPITAL

WASHINGTON, D. C.

April 1952

VOLUME VIII NUMBER 4

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AUREOMYCIN IN THE TREATMENT OF INFLUENZAL MENINGITIS

A Comparison of Therapy in 54 Consecutive Cases Over A 3 Year Period

Joseph M. McGovern, M.D.
John P. McGovern, M.D.
Sidney Ross, M. D.
E. Clarence Rice, M.D.
Frederic G. Burke, M.D.

A recent survey of meningitis at the Children's Hospital, Washington, D. C. revealed that influenzal meningitis had become the most frequently encountered type. During the three year period (1948–1950) covered by this study, there were 130 patients with meningitis admitted to the Children's Hospital, of which the etiology of 54 was the bacillus H. influenzae type B. The relative position of influenzal meningitis, with respect to the other meningidities admitted during the period of this study, is shown on Table I.

Schwachman and Kennell[1] in a recent review of the treatment of meningitis in childhood, state that "in our community (Boston), meningitis due to *Hemophilus influenzae* type B is the most common type seen, except in epidemic years when meningococcic meningitis leads." These observations vary considerably from reports of the incidence of etiology of meningitis in childhood found in the literature of previous decades, both in our own and other areas. Table II shows these earlier comparisons.

Both because of the relative and absolute increase in frequency of influenzal meningitis and the improved results in treatment with newer forms of therapy, we felt that this brief report of our findings would be of interest. The literature contains relatively few reports of the treatment of this disease with aureomycin alone or in combination with other drugs.

MATERIAL AND METHOD

The 54 cases studied fell into two distinct groups with respect to treatment. During 1948 and 1949, the drugs routinely employed were penicillin, sulfadiazine, streptomycin, and type specific (rabbit), antiserum in various combinations. There were 30 consecutive cases treated in this manner. In 1950, aureomycin became available for clinical evaluation and 24 consecutive patients received it with various combinations of the above mentioned drugs. The patients in both groups were exposed to similar diagnostic evaluation and general supportive measures.

Since the material is presented as a retrospective comparison with inherent limitations, an attempt was made to eliminate the varying severity of illness as a factor that could have, a priori, weighed one treatment group

TABLE I

Meningitis in Childhood

Children's Hospital, Washington, D. C., 1948–50—131 Cases

	CASES	MALE	FEMALE	WHITE	COLORED	AVERAGE AGE IN YEARS
Influenzal	54	27	27	40	14	2.1
Meningococcic	26	15	11	20	6	2.7
Pneumococcic	12	8	4	6	6	2.2
Etiology Unknown	12	7	5	8	4	4.7
Tuberculous	11	7	4	2	9	2.5
Lymphocytic Choriomeningitis	7	4	2	5	1	7.0
Mumps Encephalitis	4	4	0	3	1	6.0
Streptococcic	2	0	2	2	0	2 wks.
Escherichia Coli	1	0	1	0	1	1 wk.
Mixed	1	1	0	1		9 mos.
Total	130					

This table shows that influenzal meningitis is the most common type of meningitis seen at The Children's Hospital, Washington, D. C., in recent years.

TABLE II

Incidence of Meningitis by Etiology—1913–46

	NEW YORK CITY, NEW YORK NO DATE	HARRIET LANE HOME, BALTIMORE 1918–35	HOSP., SICK CHILDREN, TORONTO 1919–46	ST. LOUIS, MISSOURI 1918–35	CHIL.'S HOSP., BOSTON 1921–38	CHIL.'S HOSP., DETROIT 1929–35	CHIL. HOSP., D. C. 1924–33
Tuberculous	471	398	413		290	34	114
Meningococcic	382	274	317	160	160	48	58
Pneumococcic	43	115	195	62	69	14	35
Influenzal	33	67	191	54	78	20	58
Streptococcic	37	39	183	74	69	25	35
Staphylococcic	7	19	26	22		3	4
Totals	973	919	1325	272	705	153	331

This table indicates that influenzal meningitis in past decades was the third or fourth most common type of meningitis.

against the other. To do this, both groups were analyzed for comparability with respect to age, duration of signs and symptoms before admission to the hospital, and clinical evaluation on admission. Table III shows this comparison between the two groups.

The group that did not receive aureomycin had an average duration of signs and symptoms for 2.6 days before admission; 23 per cent appeared critically ill upon admission, while 38 per cent were 1 year of age and under. The aureomycin treated group had an average duration of signs and symptoms for 4.4 days before admission; 38 per cent appeared critically ill on admission, while 30 per cent were 1 year of age and under. These findings would indicate that before therapy was begun, the average severity of illness in the group of patients who received aureomycin was probaby at least as great as in the group which did not receive aureomycin.

In both groups, the method of administration and the amounts of therapeutic agents used were essentially the same with the exception of the addition of aureomycin in the one group. That is, intramuscular penicillin was used in doses ranging between 2,000,000 and 7,000,000 units daily in divided doses for from 1 to 5 days. In the majority of cases, penicillin was discontinued after 30 to 36 hours, by which time the *H. influenzae* type organism had been definitely identified by culture. In a few cases, however,

TABLE III

Comparison of Groups Treated With and Without Aureomycin with Respect to Age and Severity of Illness on Admission

	SIGNS AND SYMPTOMS PRIOR TO ADMISSION IN DAYS	PER CENT OF CASES CRITICALLY ILL ON ADMISSION	PER CENT OF CASES 1 YEAR OF AGE AND UNDER
24 cases treated with aureomycin	4.4	38	30
30 cases treated without aureomycin	2.6	23	38

large doses were employed for several more days. Sulfadiazine was employed in doses of 1½ to 2½ grains per pound of body weight in divided doses over a 24-hour period (0.22 to 0.36 grams per kilogram per day) intravenously or subcutaneously until adequate (10–15 milligrams per 100 milliliters) blood levels were reached and maintained. The oral route was substituted when vomiting had stopped and, fluids were being taken well by mouth, usually by the fourth or fifth hospital day. Streptomycin was administered intrathecally in amounts of between 25 and 50 milligrams on alternate days for three doses, while the concomitant daily intramuscular administration of 1 gram per day was carried out for a maximum of 10 days. When type specific antiserum was used, the initial dose was 200 milligrams (expressed as agglutinin antibody nitrogen) and when indicated, subsequent doses of serum were given in 25 to 100 milligram increments. Aureomycin was given intravenously in divided doses in amounts of 30 milligrams per kilogram of body weight each 24 hours for the first 48 hours. The oral administration of 40 to 60 milligrams of aureomycin per kilogram in divided doses, each 24

hour period, was then employed for the next 10 to 12 days, by which time criteria for discontinuance had been reached in all cases.

RESULTS

Table IV shows the results of the various combinations of treatment.

Comparative figures in each treatment group reveal that the average duration of hospital stay for those patients who did not receive aureomycin was 21 days and was 14 days for those patients who received aureomycin. The average duration of temperature elevation above 100 F. was 4 days in the aureomycin treated group in contrast to 7 days in the comparison group.

TABLE IV

Influenzal Meningitis at the Children's Hospital, Washington, D. C., 1948–50; Comparison of Results of Fifty-four Cases Treated With and Without Aureomycin

	NO. OF CASES	DURATION OF HOSPITAL STAY IN DAYS	AVERAGE DURATION OF TEMPERATURE ELEVATION ABOVE 100 F. IN DAYS
Sulfadiazine, Serum, Streptomycin	20		
Sulfadiazine Streptomycin	9	21	7
Serum, Streptomycin	1		
Total	30		
Sulfadiazine, Serum, Streptomycin, Aureomycin	2		
Sulfadiazine Aureomycin	12	14	4
Sulfadiazine, Streptomycin, Aureomycin	9		
Sulfadiazine, Serum, Aureomycin	1		
Total	24		

There were 11 patients in the group without aureomycin whose spinal fluid was still positive for *H. influenzae* type B beyond the third hospital day; whereas, no patients in the aureomycin treated group had positive spinal fluid cultures beyond the third hospital day. An example is seen in table V.

Complications developed in 13 patients not receiving aureomycin as contrasted with 6 patients treated with aureomycin. The complications noted upon discharge from the hospital included: deafness, ataxia, hemiparesis, hemiplegia, hydrocephalus, convulsive disorders, and disturbances in behavior. Table VI shows the number of patients who developed complications and the mortality rate in per cent.

Since the recent observation of McKay[2] and Smith[3], that subdural effusion is a frequent complication of pyogenic meningitis, routine performance of subdural punctures in all patients with pyogenic meningitis has become a standard procedure at the Children's Hospital. As a result, we expect that in the future, a greater number of patients with this complication will be recognized. In the present series, a subdural effusion was found in the only patient on whom a subdural tap was performed. Although sufficient time has not elapsed for complete follow-up studies, analysis of the available data indicates that transient deafness and ataxia accounted for the greater incidence of complications among the group that did not receive

TABLE V

Influenzal Meningitis at the Children's Hospital Washington, D. C., 1948–50; Comparison of Results of Fifty-four Cases Treated With and Without Aureomycin with Respect to Speed of Sterilization of Cerebrospinal Fluid

Number of Patients Whose Cerebrospinal Fluid Culture Was Positive for *H. Influenzae* Type B After the Third Hospital Day

30 Cases—Total: Group treated with conventional measures (Serum, Sulfadiazine, Streptomycin)	11
24 Cases—Total: Group treated with conventional measures (Serum, Sulfadiazine, Streptomycin), plus Aureomycin	0

TABLE VI

Influenzae Meningitis at the Children's Hospital Washington, D. C., 1948–50; Comparison of Results of Fifty-Four Cases Treated With and Without Aureomycin With Respect to Incidence of Complications and Mortality Rate

	NUMBER OF PATIENTS WHO DEVELOPED COMPLICATIONS	MORTALITY RATE IN PER CENT
Group treated with conventional measures (Serum, Sulfadiazine, Streptomycin)	13	12
Group treated with conventional measures (Serum, Sulfadiazine, Streptomycin), plus Aureomycin	6	12

aureomycin. It is felt that this type of complication was due for the most part to toxic effects of streptomycin which was used with greater frequency and for longer periods in that group. No severe toxic reactions were noted with the dosage of aureomycin employed in the present series. However, several patients developed transient phlebitis at site of injection. The mortality rate in both groups was the same (12 per cent).

It is of interest to note that 2 of the patients who died presented the clinical picture of acute adrenal insufficiency, and at autopsy, bilateral hemorrhage and necrosis of the adrenal cortex was observed, suggesting a Waterhouse-Friderichsen Syndrome.

DISCUSSION

Before the advent of sulfonamides and type specific *H. influenzae* (rabbit), antiserum developed by Alexander, *Hemophilus influenzae* meningitis was a highly fatal disease with a 90 to 100 per cent mortality in most of the reported series. With this improved therapy and the later addition of streptomycin, the mortality declined to from 10 to 20 per cent in a series of cases collected and reported in 1946 by the National Research Council[4].

Reports from abroad have indicated that large doses of penicillin seem to be efficacious in the treatment of this disease[5]. In the present series, penicillin was generally not used once H. influenzae had been positively identified. No conclusions can be drawn regarding the advisability of its use since only a few cases were treated with it.

A review of the literature revealed only 15 reported cases of *H. influenzae* type B meningitis treated in this country with aureomycin alone or in combination with other drugs. There was 1 death reported among these 15 cases[6, 7, 8, 9].

McCrumb et al[10] found aureomycin and streptomycin to be equally effective in the chemotherapy of *H. influenzae* infections in mice and that protection afforded by chloromycetin, although slightly less, was, nevertheless, significant. Long[11] and Hardy[12] consider aureomycin to be highly effective in the treatment of *H. influenzae* meningitis, especially when used in combination with sulfadiazine.

In our group of 24 patients who received aureomycin in addition to therapeutic agents of previously proven value, streptomycin, sulfadiazine, and type specific antiserum, the mortality rate was 12 per cent. Although this mortality rate is the same as that of the group of 32 patients treated with sulfadiazine, streptomycin, and antiserum, nevertheless, we feel that aureomycin has a place of distinct value in the treatment of this disease.

The results indicate that the addition of aureomycin seems to effect a more rapid clinical response, a more rapid sterilization of the cerebrospinal fluid and a shortening of the hospital stay. Furthermore, aureomycin is superior to streptomycin in that it does not present the hazard of eighth nerve damage, and is not so likely to produce resistant strains of organisms as is the case with streptomycin.

The advisability of employing sulfadiazine and type specific (rabbit), antiserum in conjunction with aureomycin is a question that has not been adequately evaluated as yet.

It should be pointed out that chloromycetin has also been used in the treatment of *H. influenzae* meningitis with satisfactory results[13, 14, 15].

Our results in the treatment of *H. influenzae* type B meningitis with chloromycetin will be the subject of a forthcoming paper.

It is not generally recognized that a Waterhouse-Friderichsen type of syndrome can occur due to the *H. influenzae* type B organism. Our ex-

perience with one case suggests that total eosinophile counts should be used routinely to provide warning of impending adrenal cortical failure. Should the total eosinophile count be abnormally high, large doses of adrenal cortical extract, 50 to 100 milliliters every 4 hours should be administered together with cortisone by the intravenous route.

SUMMARY

1. A series of 54 cases of *H. influenzae*, type B meningitis is presented.

2. Thirty patients received various combinations of sulfadiazine, streptomycin, and type specific (rabbit) antiserum with a mortality of 12 per cent.

3. A comparable group of 24 patients received various combinations of sulfadiazine, streptomycin, and type specific antiserum with the addition of aureomycin, also with a mortality rate of 12 per cent.

4. One case in this series was proven at autopsy to have Waterhouse-Friderichsen Syndrome.

5. In the aureomycin-treated group of patients, the clinical response was more rapid and complete and there were fewer complications observed than in the group that did not receive aureomycin.

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KARTAGENER'S TRIAD

Case Report No. 228

Richard J. Maher, M.D.

Kartagener's triad consists of dextrocardia, bronchiectasis, and sinusitis. The reporting of a patient exhibiting these abnormalities seems desirable in view of the rarity of the condition. The case reported herein represents a classical example of this syndrome.

CASE REPORT

N. D., a ten-year-old white female, was admitted to Children's Hospital on December 6, 1951 because of chronic cough.

The child was born after a full term pregnancy and normal labor following which the attending physician thought she had pneumonia because of excessive secretions of mucus from the nose. She did well until the age of two years except for the continued secretions mentioned above and "rattling" in the chest. After this she failed to gain weight, had poor appetite, cried frequently, and had frequent upper respiratory infections. Roentgenographic examination, at that time, showed dextrocardia with situs inversus. Pneumonia occurred two years later, at which time a diagnosis of bronchiectasis was made. At seven years of age, the patient's appetite improved; she gained in height and weight, and improved generally. However, chronic cough with large amounts of sputum which occasionally was blood streaked continued to be a problem. At this time it was noted that the patient fatigued easily, had developed ear infections, and continued to have thick, purulent nasal secretions. The family physician believed that the patient was becoming deaf. Of importance was a history of enuresis and the refusal of the patient to attend school because of the embarrassment caused by excessive coughing.

Of the five siblings, none was affected with respiratory disease. One was thought to have possible heart disease of unknown etiology. A history of diabetes, epilepsy, and allergy in other relatives was obtained.

Physical examination: height, 58 inches; weight, 83 pounds; temperature, 98.6 F.; pulse, 84; respirations, 20. The child appeared to be very well developed and well nourished for her age. Positive findings included tonsillar enlargement with follicular exudate; flattened, depressed left chest; dextrocardia; dullness, decreased breath sounds and inspiratory rales at both bases; left-sided liver; right-sided stomach bubble, and marked clubbing of the fingers. A frequent cough was productive of purulent, non-bloody sputum.

Laboratory data included: hemoglobin, 11.8 grams; red blood cells, 4,200,000; white blood cells, 17,500; differential, segmented forms 65, band forms 4, young forms 2, lymphocytes 25, monocytes 2, eosinophiles 1, and basophiles 1 per 100 white blood cells. Urinalysis was normal. The fasting blood sugar was 80 milligrams per 100 milliliters. Sputum culture showed pneumococcus, type undetermined.

Roentgenographic examination of the chest showed dextrocardia with situs inversus and pulmonary changes consistent with bronchiectasis. Examination of the nasal accessory sinuses disclosed a pan-sinusitis. Bronchographic examinations revealed cystic bronchiectasis involving the right base with small, chopped-off bronchi in the left lung indicative of early bronchiectasis on that side.

Course in the hospital: The child proved to be extremely uncooperative and immature, failing to adjust herself to the necessary diagnostic and therapeutic measures. All attempts at postural drainage, inhalation therapy, and other therapeutic procedures were unsuccessful because of the lack of cooperation. She was discharged from the hospital at the mother's request to be followed in the thoracic clinic of a neighboring hospital.

DISCUSSION

A perusal of the English-language literature shows that this syndrome or triad was first clearly established by Kartagener. He has written a number of articles on the subject. Adams and Churchill[1] noted that 5 of 23 patients

with dextrocardia had bronchiectasis. They contrast this incidence of 21.7 per cent with an incidence of 0.306 per cent for bronchiectasis in general hospital admissions and an incidence of 0.002 per cent for dextrocardia. Coll and Nalls[2] reported a case of this disease in 1940. Olsen[3] studied 85 cases of dextrocardia with situs inversus, and of these, 14, or 16.5 per cent, had bronchiectasis. Ten of the 14 cases of bronchiectasis showed definite disease of the nasal sinuses. Of the 85 cases without bronchiectasis 4 showed sinus disease. They also contrasted the incidence of bronchiectasis in general hospital admissions and emphasized the much higher incidence when associated with dextrocardia. Another interesting feature of their study was that of these 85 patients there were 11 with other types of congenital disease: heart disease, hydrocephalus, imperforate anus, cleft palate, polydactylism, flail thumb, and others were mentioned. None of the patients with bronchiectasis had any other congenital defects. They postulate that the bronchiectasis and sinusitis are due to a congenital weakness of the entire respiratory tree which renders the individual susceptible to infection. Andrews[4] reported a case with congenital absence of the perinasal sinuses. This patient was deaf, had small frontal sinuses, poor ethymoid labyrinths, small and poorly developed antra, and had no air cells in either mastoid area.

One gathers from the literature on the subject that the most commonly accepted explanation of this syndrome of bronchiectasis and sinusitis is that offered by Olsen[3]; namely, congenital weakness of the entire respiratory tree and increased susceptibility to infection. The recommended treatment includes the usual medical and surgical methods of management. Had our patient been more cooperative, a better result might have been obtained; however, the refusal of the family and child to accept therapy leaves this a very moot point.

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CHRONIC MYELOCYTIC LEUKEMIA IN CHILDHOOD

Report of a Case

Case Report No. 229

Sanford Leikin, M.D.
Richard J. Waters, M.D.

In children myelocytic leukemia of the chronic type is an uncommon but not rare form of blood dyscrasia. In 1933 Eisenberg and Wallerstein[1] collected 30 cases of this disease and added one of their own. Cooke[2], in 1934, stated that he observed three cases of chronic myelocytic leukemia in children eight, nine, and twelve years of age during fifteen years at the St. Louis Children's Hospital. Recently he[3] has stated that approximately 5 per cent of cases of leukemia in children are of this form. Wintrobe[4] describes a six year old boy who was known to have had classical chronic myelocytic leukemia for 22 months. Sullivan[5] et al classified one child living 15 months as having this entity. In an analysis by Shimkin[6] et al on myelocytic leukemia, a graph concerning onset shows that there was one patient below the age of 10 years and one from 10 to 15 years of age seen in the three San Francisco Hospitals which were surveyed between the years of 1910 and 1948.

Several cases of chronic myelocytic leukemia of congenital origin in infancy have been described lately[7, 8, 9, 10]. Chronic lymphocytic leukemia is extremely rare in infancy.

The clinical picture is similar to that in adults with weakness, lassitude, and pallor. A very striking feature of the history in a large majority of cases is the presence of numerous infections, not infrequently with one infection following immediately upon another.

The spleen is always markedly enlarged while hepatic enlargement varies from slight to very marked; adenopathy is not a frequent or a prominent sign, and neither is fever.

The blood picture in chronic myelosis demonstrates high leukocytosis, the immature granulocytes (metamyelocytes, myelocytes, promyelocytes, and myeloblasts) with an increase in eosinophiles and basophiles. In children there is a greater frequency in the appearance of the youngest or myeloblast forms. This is probably to be accounted for by the greater irritability of the hemopoietic system in children. The aleukemic form of the disease is quite rare. Anemia is always present and frequently is quite severe. Paradoxically, the thrombocyte count may be increased.

Prognosis as to life is hopeless, and as to duration, variable, —some patients living as long as five and six years; while others, especially those with a sub-leukemic count, survived from a few months to two years.

CASE REPORT

J. C., an eight year old white male was admitted to Children's Hospital, Washton, D. C. on September 30, 1950 with the complaint of poor vision. The patient always had had a protuberant abdomen, and for the last year previous to admission, he tired easily. For two or three months it had also been noted that he had many bruises which were attributed to falls from his bicycle. The day prior to admission the patient's teacher informed his mother that he had had trouble seeing in school for the last month. The child was then brought to an ophthalmologist who referred the patient to a pediatrician.

The family history was non-contributory as was the past history.

Physical examination on admission revealed a well developed, well nourished pale boy with puffiness around the eyes, who was not in acute distress. The temperature was 102.0 F. (R). There were several ecchymotic areas on the skin of the buttocks and legs. The anterior cervical and inguinal nodes were slightly enlarged. Examination of the eyes showed equally dilated pupils. The fundus oculi showed a few whitish plaques in the periphery, some of which are surrounded by a whitish halo and areas of retinal hemorrhage.

On percussion, the cardiac left border dullness extended 2 centimeters to the left of the midclavicular line and auscultation revealed a grade III blowing systolic murmur heard over the entire precordium loudest in the pulmonic region. The lungs were negative to percussion, but there were a few ronchi at the left base on auscultation.

The spleen, which was firm and smooth, could be palpated in the left quadrants of the abdomen and extended to the left iliac fossa and to the right of the midline. The liver was also palpable 2 centimeters below the right costal margin.

The extremities were normal and the neurological examination showed no abnormalities except for the fundoscopy which was mentioned above.

The admission hemogram revealed hemoglobin 8.0 grams; red blood cells 2,690,000 per cubic millimeter; white blood cells 508,000 per cubic millimeter and the total platelet count was 49,500 per cubic millimeter. The differential white count showed 4 per cent neutrophilic promyelocytes, 24 per cent neutrophilic myelocytes, 7 per cent neutrophilic metamyelocytes, 6 per cent neutrophilic bands, 32 per cent neutrophilic segmented cells, 9 per cent eosinophilic segmented cells, and 17 per cent basophilic segmented cells. There was a reduction in the number of thrombocytes seen and some hypochromia, anisocytosis, and poikilocytosis of the red cells on the smear. The urine was normal. Roentogengrams of the chest showed slight cardiac enlargement to the left. X-ray of the lower extremities, pelvis, sacrum and coccyx, hips and upper portion of the femora revealed no evidence of fracture or any other osteal or periosteal pathology.

On October 5, 1950, urethane therapy was instituted in a dosage of 1.0 to 2.5 grams per day for 19 days. Six blood transfusions were given during this same period. No beneficial effects were noted during this time except for improvement in his vision which occurred several days after admission.

Because of the poor response to urethane, deep x-ray therapy to the spleen was started on October 23, 1950 and given in a dosage of 135 roentgens per day for nine days. He was discharged on October 30, 1950 to be followed as an outpatient. At this time he was active, asymptomatic; his spleen had decreased in size so that its tip was palpable 10 centimeters below the left costal margin and his hemogram showed 3,000,000 erythrocytes per cubic millimeter with 12 grams of hemoglobin. The total thrombocyte count was 290,000 per cubic millimeter and there were 106,000 leuko-

cytes per cubic millimeter. The differential count showed 5 per cent neutrophilic myelocytes, 6 per cent neutrophilic metamyelocytes, 45 per cent neutrophilic bands, 41 per cent neutrophilic segmented cells, 1 per cent eosinophilic segmented cells, 1 per cent basophilic segmented cells, and 1 per cent adult lymphocytes. The peripheral smears showed normal platelets and red blood cells.

The patient's condition remained good for about two weeks, however on November 17, it was noted that he had become pale and had developed petechiae and ecchymosis

FIG. 3. Before treatment

on the legs and face. His red blood count was 3,500,000 per cubic millimeter with 10 grams of hemoglobin per 100 milliliters of blood. His leukocyte count had dropped to 10,500 with 97 per cent granulocytes and 3 per cent adult lymphocytes (See Table I). His thrombocyte count was 43,000 per cubic millimeter. He was readmitted to the hospital and erythrocyte, leukocyte, and thrombocyte counts continued to drop in spite of six transfusions given over the next two-week period. Examinations done on the patient's blood showed a negative Coombs test, and red cell fragility showed hemolysis of the patient's cells beginning at 0.46 per cent saline solution and ending at

TABLE 1

Summary of Blood Studies and Therapy

DATE	RBC	HB	WBC	PLATE-LETS	BLAST	NEUTROPHILIC					LYMPH	ATYP	MONO	EOS SEGS	BAND SEGS	TREATMENT
						Pro.	Myel.	Young	Band	Seg.						
9-30-50	2.6	8.0	508,000	49,500		5	24	7	6	32				9	17	
10-3 -50																300 ml. blood
10-5 -50																*
10-6 -50																300 ml. blood
10-10-50																300 ml. blood
10-12-50	2.2	7.5	460,000	164,000	2	16.5	11	18.0	13	19.5	6.0			5	8.5	300 ml. blood
10-18-50																300 ml. blood
10-20-50	3.0	10.0	620,000													300 ml. blood
10-23-50																X-ray (135 r)
10-24-50																X-ray (135 r)
10-25-50																X-ray (135 r)
10-26-50																X-ray (135 r)
10-27-50																X-ray (135 r)
10-30-50	3.9	12.0	106,000	290,400			4	6	45	41	1			1	1	X-ray (135 r)
10-31-50																X-ray (135 r)
11-1 -50			55,000		1		1	11	43	34	3			1	6	X-ray (135 r)
11-2 -50																X-ray (135 r)
11-17-50	3.5	10.0	10,500	43,000			1	1	1	91	3			3		300 ml. blood
11-24-50																300 ml. blood
11-25-50																300 ml. blood
11-26-50																300 ml. blood
11-28-50																300 ml. blood
11-30-50																300 ml. blood
12-2 -50	3.8	9.5	900	89,000												300 ml. blood
12-3 -50																Adrenalin hydrochloride 0.2 ml. S. Q.
12-4 -50																Typhoid ⊕ 0.3 subcutaneously
12-6 -50	3.4	10.5	1,300				4		7	48	39					Typhoid ⊕ 0.1 intravenously
12-8 -50																Typhoid ⊕ 0.3 intravenously
12-9 -50																300 ml. blood
12-11-50																300 ml. blood
12-14-50																300 ml. blood
12-16-50																300 ml. blood
12-18-50																300 ml. blood
12-19-50	4.8	14.0	3,200	120,000					15	44	34			5	2	
1-2 -51	2.8	9.5	6,500	56,000	1			5	10	66	15			3		300 ml. blood
1-16-51																300 ml. blood
1-26-51	2.9	9.5	4,500	135,000					8	56	34	2				
2-1 -51																300 ml. blood
3-3 -51	3.4	10.5	4,900	99,000				5	22	41	26			4	2	
3-24-51	3.8	12.5	7,100	118,000					6	68	25				1	
5-12-51	4.0	12.0	7,700	191,000					9	57	21		1	9	3	
1-19-52	3.5	12.0	13,900	normal					2	72	20		2	3	1	

* Urethane (1.0–2.65) administered from: 10–3–50 to 10–23–50. ⊕ Vaccine

0.34 pre cent; control cells started to hemolyze at 0.44 per cent and ended at 0.32 per cent. The total biliruinb was 0.6 milligrams with an indirect bilirubin of 0.48 milligrams and direct of 0.12 milligrams. On December 1, an adrenalin tolerance showed-

no essential change in the corpuscular elements and typhoid vaccine, given subcutaneously and intravenously a few days later, showed no beneficial effects.

From December 2 to December 19, another six blood transfusions were given and on December 23 the patient was discharged to his parents in an improved condition. At that time he was active and his appetite was good. There were no hemorrhagic manifestations and his spleen was palpable 6 centimeters below the left costal margin. The patient's hemogram was improved (See Table I).

FIG. 4. Shortly after the cessation of urethane and x-ray therapy

During January of 1951 the patient continued to do fairly well at home, however, it was necessary to give four blood transfusions to maintain his blood count in good condition.

Since that time his condition has remained good. He contracted varicella and several respiratory infections without any untoward complications. His spleen has remained palpable from 1 to 6 centimeters below the left costal margin and the liver from 2 to 3 centimeters below the right costal margin. He has shown no severe hemorrhagic tendencies.

TABLE II

	ILIAC BONE MARROW EXAMINATIONS					
	1-2-50	11-17-50	1-24-51	4-4-51	8-31-51	12-4-51
Leukoid:Erythroid Ratio	120:1	12:1	5:1	13:1	5:1	12:1
Myeloblasts (%)	2			1	0.25	1
Promyelocytes (%)						
Neutrophilic	6		0.5	0.5	1.5	4
Myelocytes (%)						
Neutrophilic	12		4.5	1.5	14.75	10
Eosinophilic	3			0.5		
Basophilic						
Metamyelocytes (%)						
Neutrophilic	24	3	13	7	12.5	11
Eosinophilic	9	1	2	1.5	0.5	
Band Forms						
Neutrophilic	20	24	30	22	28.75	33
Eosinophilic				1.5	1.0	
Segmented Forms						
Neutrophilic	11	58	14	44	31.5	33
Eosinophilic	4	4	1	5.5	1.0	3
Basophilic	5	2			.75	2
Prolymphocytes					2	
Atypical Lymphocytes				.5		
Adult Lymphocytes	4	8	37	16.5	5.5	3
Megakaryocytes	reduced	reduced	reduced	not seen	normal	normal

COMMENT

It is difficult to say how long the patient had leukemia when first seen by us, but apparently it was an advanced disease process when the diagnosis was first made. He has now been observed with chronic leukemia for sixteen months.

The severe pancytopenia which occurred was probably due to an excess of roentgenotherapy. Forkner[11] warns that x-ray and radium therapy should be undertaken cautiously in children since they respond to much smaller doses than adults.

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CAUSES OF DEATH DURING 1951 BASED ON FINDINGS AT NECROPSY

A survey from January 1 through December 31

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Ruth Lau, M.D.

During 1951 there were 123 deaths among the 9786 patients admitted to the children's hospital of the District of Columbia for treatment. Table I shows the corrected number and percentage of necropsies performed.

Table II summarizes the causes of death listed in Table I, based chiefly on the major pathology findings at necropsy.

TABLE I

Total hospital deaths		123
Autopsies performed		108
Courtesy autopsies	3	
Autopsies at hospital on patients dead on arrival	5	
Corrected number of autopsies		100
Autopsy percentage*		85.5%

* Corrected for coroner's cases.

Table III lists the total number of deaths due to the various causes arranged in order of frequency. As in the previous year, infections and congenital anomalies continue to predominate. However, deaths resulting from infection have dropped approximately 10 per cent. This decline may be due to the increased availability of antibiotics and chemotherapeutic agents and their more specific use.

Among the 32 cases classified under the heading of infection in Table III; the causative organism was isolated in 50 per cent. In the remaining half, mixed infections made it impossible to definitely determine the responsible organism and the majority of the pulmonary infections are believed to belong to this group.

Of those who died following an operative procedure, the classification cannot be made sharply as to whether the patients died of the orginal dis-

TABLE II

Congenital Anomalies		20
Brain	3	
Cerebral cyst	1	
Hydrocephalus Cerebral Agenesis	2	
Heart	13	
Cor bilocularis	1	
Single ventricle	1	
Tricuspid atresia	1	
Tetralogy of Fallot	2	
Truncus arteriosis	1	
Transposition of great vessels	2	
Post-ductal coarctation	2	
Anomaly of systemic venous return	1	
Anomaly of pulmonary venous return	1	
interventricular septal defect	1	
Biliary Anomaly	1	
Alimentary Tract	3	
Tracheo-esophageal fistula	2	
Sigmoido-urethral fistula with pyloric hypoplasia	1	
Infection		32
Brain Abscess	2	
Staphylococcus	1	
Klebsiella pneumoniae, type b	1	
Meningitis	4	
H. influenzae	2	
N. meningitidis	1	
M. tuberculosis	1	
Laryngotracheo Bronchitis	3	
H. influenzae	1	
Klebsiella pneumoniae	1	
Unclassified	1	
Pulmonary Infection	8	
Lobar pneumonia	2	
Bronchopneumonia	1	
Aspiration pneumonia	1	
Alveolitis	1	
Undetermined	2	
Bronchiolitis	1	
Mediastinitis (Due to perforation of esophagus)	2	
Hepatitis, cause undetermined	1	
Generalized Infection	12	
H. influenzae	1	
N. meningitidis—with bilateral adrenal hemorrhage	2	
M. tuberculosis	3	
H. pertussis	1	
C. tetanus	1	
Undetermined	4	
Malignant Tumors		4
Glioblastoma	1	
Osteogenic Sarcoma	1	
Anaplastic Carcinoma of Pancreas	1	
Leukosarcoma	1	

TABLE II—*Continued*

Diseases of the Blood Forming Organs		4
Leukemia, Lymphocytic	3	
Erythroblastosis	1	
Diseases of the Reticulo-Endothelial System (Letterer-Siwe's Disease)		1
Endocrine Diseases		2
Adreno-genital Syndrome	2	
Metabolic Diseases		3
Von Gierke's Disease (Hepatic Type)	1	
Diabetes mellitis	2	
Degenerative Diseases		2
Schilder's Disease (Encephalitis peri-axialis diffusa)	1	
Dermatomyositis	1	
Poisoning		2
Salicylate	1	
Veratrum Viride	1	
Renal Diseases		4
Pyelonephritis, Chronic	1	
Glomerulonephritis:	3	
Diffuse, Chronic	1	
Early, proliferative	1	
Nephrotic stage	1	
Immaturity		1
Injuries		7
Resuscitation	2	
Pneumothorax	1	
Pulmonary hemorrhage	1	
Burn	1	
Foreign Body Obstruction	1	
Traumatic	3	
Brain	2	
Intestinal perforation	1	
Operative Complications		10
Peritonitis	7	
Post-craniotomy (astrocytoma)	1	
Post-ileocolostomy	1	
Post-appendectomy	2	
Post-colostomy	1	
Post-nephrectomy	1	
Post-diaphragmatic herniorrhaphy	1	
Death during operation—Gliotomy (Congenital glaucoma)	1	
Death During Anesthesia—Muscle Biopsy (Von Gierke's disease, cardiac type)	1	
Post-Cystectomy, Undetermined (Rhabdomyosarcoma of Bladder)	1	
Intracranial Hemorrhage		2
Intraventricular Hemorrhage	1	
Subdural Hematoma	1	
Unclassified Diseases		5
Endocardial Fibroelastosis of the heart	1	
Idiopathic Hypertrophy of the heart	1	
Mongolism	2	
Hirschsprung's Disease	1	

ease or whether the deaths were due to the operation. The evaluation of the leading causes of death listed inTable II are based on the duration between the operation and death, the severity, and the extent of damage done by the original disease. Nevertheless, a number of ambiguous cases have been encountered; for instance, two of the patients with congenital heart disease who died shortly after operation were classified under the congenital anomaly because the patients were in apparent cardiac failure before operation

TABLE III

Infections	32
Congenital Anomalies	20
Operative Complications	9
Injuries	7
Malignant Tumors	4
Blood Diseases	4
Renal Diseases	4
Metabolic Diseases	3
Endocrine Diseases	2
Degenerative Diseases	2
Poisoning	2
Intracranial Hemorrhage	2
Immaturity	1
Diseases of Reticulo-Endothelial System	1
Unclassified	5
Total	100

TABLE IV

TYPE OF OPERATIVE COMPLICATION	ORIGINAL DISEASES	REARRANGED CLASSIFICATION
Death during Gliotomy	Congenital Glaucoma	Congenital Anomaly
Death during anesthesia—muscle biopsy	Von Gierke's disease, cardiac type	Metabolic disease
Post craniotomy	Astrocytoma	Tumor, benign
Post cystectomy	Rhabdomyosarcoma of bladder	Tumor, malignant
	Tetralogy of Fallot	Post Blalock operation
	Tricuspid atresia	Post-Pott's operation

proceeded. Among the 10 deaths due to operative complications, four patients had diseases which carry poor prognosis, but because of the unexpected death during or after operation, these instances were grouped under the heading of the operative complications rather than under their original diagnosis. Had these ambiguous cases been rearranged according to their original diseases, the statistics given in Table III would be slightly altered. Table IV gives the alternate classification of these ambiguous cases.

OBITUARIES

Dr. Custis Lee Hall

On November 10, 1951, orthopedic surgery in particular, and medicine in general lost a valuable member. Dr. Custis Lee Hall was born in Washington, D. C. in 1888 and was graduated from the George Washington School of Medicine in 1921. He interned at the Garfield Memorial Hospital and had his orthopedic training at the Massachusetts General Hospital in Boston. Dr. Hall was overseas during the first World War as an orthopedic surgeon. He was largely responsible for the status of orthopedic surgery as it exists today in Washington. He was a stimulating teacher and very unselfish with his knowledge. His devotion to the crippled child was unparalleled, and for years he served in the Orthopedic Clinic at the Children's Hospital. Dr. Hall was widely traveled and very instrumental in the American Chapter of the International College of Surgeons. He was personally acquainted with the leading opthopedic surgeons throughout the world. Dr. Hall was Clinical Professor of Orthopedic Surgery at the George Washington University Hospital from 1919 until his death. He was closely connected with the teaching of orthopedic surgery in Washington. His many students will long remember him for his unselfish sharing of his knowledge. Dr. Hall was one of the founders of the Washington Orthopedic Club, and at the time of his death, was the president of that organization. He was also the past president of the American Chapter of the International College of Surgeons. He was an inspiration to the orthopedic surgeons in Washington and was never hesitant to give advice or lend a helping hand. His contributions to medical literature were numerous and his contributions to orthopedic surgery will long be remembered.

William J Tobin, M.D.

Dr. Philip Litvin

Dr. Philip Litvin, attending neurologist at Children's Hospital, was drowned on August 20, 1951, while on vacation in Montana.

Born in Latvia, November 7, 1907, the son of Benjumin and Yetta Litvin, Dr. Litvin was brought to the United States at the age of 5 years. He attended the old Addison School and McKinley High School in Washington, D. C.

In 1929 he was graduated from George Washington University School of Medicine, interning the following year at Garfield Memorial Hospital. He was physician to the United States Soldier's Home Hospital from 1930 to 1936. He received a law degree from Southeastern University in 1940.

Dr. Litvin limited his practice to neurology and psychiatry, with offices at 2023 Q Street, N. W. He was a psychiatrist for the District Commission on Mental Health.

During World War II, he was a neuropsychiatrist in the Medical Corps of the United States Army, serving at several Army installations, and was discharged after four years of service with the rank of lieutenant colonel.

He was a Fellow of the American Medical Association and an active member of the District Medical Society Service 1938, a member of the American Psychiatrist Association and of the Medical Society of Saint Elizabeth's Hospital.

At the time of his death he was a member of the senior staff of Garfield Memorial Hospital and Children's Hospital and on the visiting staff of Gallinger Municipal Hospital. He was also Associate Professor of Neurology at Georgetown University School of Medicine.

Surviving are his wife, Mrs. Fanney Neyman Litvin, his mother, and three brothers, Morris, Aaron and Abraham Litvin.

Dr. Litvin was an able, kindly and helpful colleague, and his presence will be sorely missed.

EDWARD LEWIS, M.D.